REMARKS

According to the Office Action of November 25, 2009, claims 17, 20, 21, 23, and 25-28 and 30 are pending in this application. Claims 18, 19, 22, 24, 29 and 31 were previously cancelled. The pending claims stand rejected under 35 U.S.C. § 102(b) as anticipated by Place[1] as evidenced by Yamazaki[2]. In response, Applicants have amended claim 17 to incorporate the limitations recited in claim 23, and have cancelled claim 23. Thus, no new matter has been added by this amendment.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). In this case, Place does not teach each and every element of amended claim 17 because one of ordinary skill in the art would not understand testosterone as including 15-hydroxytestosterones or precursors thereof (as defined by amended claim 17).

Claim 17, as amended, is directed to a pharmaceutical oral dosage unit containing at least 10 μg of a steroid selected from the group consisting of 15-hydroxytestosterones, precursors thereof, mixtures thereof and precursors thereof said mixtures; and a pharmaceutically acceptable excipient. The oral dosage unit is selected from the group consisting of a tablet, a capsule and a chachet. The precursors of the hydroxytestosterones are derivatives of the hydroxytestosterones wherein a hydrogen atom of at least one hydroxyl group has been substituted by an acyl radical of a hydrocarbon carboxylic, sulfonic or sulfamic acid of 1-25 carbon atoms; tetrahydrofuranyl; tetrahydropyranal; or a straight or branched chain glycosydic residue containing 1-20 glycosidic units per residue. Claims 20, 21, 25-28 and 30 ultimately depend from claim 17.

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[1] U.S. Pat. No. 6,117,446 to Place ("Place").

[2] Tamazaki et al., "Progesterone and testosterone hydroxylation by cytochromes P450, 2C19, 2C9 and 3A4 in human liver microsomes", ARCHIVE OF BIOCHEM AND BIOPHYS, (Oct. 1, 1997): 161-169 ("Yamazaki").

Place teaches a buccal drug delivery system comprising an androgenic agent, a progestin, an estrogen and a bioerodible polymeric carrier.[3] The Office Action contends Place teaches employing naturally occurring androgens and derivatives thereof, such as testosterone, and that, according to Yamazaki, 15-hydroxytestosterones are naturally occurring androgens.[4]

However, one would not understand the androgen discussed in Place to include 15-hydroxytestosterone. 15-hydroxytestosterone is not a naturally occurring androgens. An androgen is a hormone that stimulates or controls the development and maintenance of masculine characteristics in vertebrates by binding to an androgen receptor. The scientific publications previously submitted establish hydroxylation of testosterone in the liver inactivates testosterone,[5] thus it no longer binds to an androgen receptor. Harada states that "[h]ydroxylation of steroid hormones and subsequent conjugation of hydroxylated steroids are also interesting biological functions of liver microsomes, pathways by which ***steroid hormones are believed to be metabolized to inactive forms***."[6] Likewise, Gustafsson states that "[i]t is speculated that the physiological role of the highly sex-specific 15β-hydroxylase system is to ascertain efficient hepatic ***deactivation*** of potential androgenic compounds in female rats."[7]

Yamazaki does not provide any information to refute this. It does not state that hydroxytestosterones bind to an androgen receptor. In fact, it expressly states that "CYP2C19 plays important roles in the oxidation of progesterone and testosterone in human liver microsomes, ***although the physiological significance of these metabolic pathways remains unclear***."[8] It further acknowledges that hydroxylation of testosterone is part of catabolism of testosterone ("Among various P450 enzymes examined CYP3A4 is shown to be one of the major

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[3] Office Action at page 3.

[4] Office Action at page 3-4.

[5] Harada *et al.*, "Mouse liver testosterone 15α-hydroxylase (cytochrome P-450$_{15\alpha}$)," J. OF BIOL. CHEM. (1984) 259(2): 1265-1271 ("Harada") (previously submitted together with the Request for Reconsideration dated September 15, 2008); Gustafsson *et al.*, "Regulation and properties of a sex-specific hydroxylase system in female rat liver microsomes active on steroid sulfates," J. OF BIOL. CHEM. (1974) 249(6): 1940-1945 (previously submitted with the Request for Reconsideration dated September 15, 2008).

[6] Harada at page 1269 (emphasis added).

[7] Gustafsson at page 1940 (emphasis added).

[8] Yamazaki at page 161.

P450 forms involved in the steroid ***catabolism*** in human livers ...."[9]), which one of ordinary skill in the art would understand to mean as the breakdown of testosterone into an inactive form. From this, one would conclude that a catabolic form of an androgen, such as a 15β-hydroxytestosterones, is not an androgen by definition.

Accordingly, Yamazaki does not evidence that 15-hydroxytestosterone are naturally occurring androgens. In contrast, it evidences that 15-hydroxytestosterone are catabolites of an androgen. Thus, Place's teaching of employing naturally occurring androgens and derivatives thereof does not include employing 15-hydroxytestosterones, precursors thereof, mixtures thereof and precursors of said mixtures, as recited in claim 17. Accordingly, claim 17 is novel over Place. For the same reasons, claims 20, 21, 25-28 and 30, which ultimately depend from claim 17, are novel over Place.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the asserted rejections, and allowance of pending claims 17, 20, 21, 25-28 and 30. Should the Examiner like to discuss this application further, the Examiner is invited to contact the Applicants' undersigned representative at (412) 471-8815.

Respectfully submitted,

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[9] Yamazaki at page 162 (emphasis added).